

Exhibit D

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

Rheinfrank, et al.,	:	
	:	Case No. 1:13-cv-144
Plaintiffs,	:	
	:	Judge Susan J. Dlott
v.	:	
	:	Order Ruling on <i>Daubert</i> Motions
Abbott Laboratories, Inc., et al.,	:	
	:	
Defendants.	:	
	:	

This is a product liability case under Ohio law arising from Plaintiff Pamela Rheinfrank’s ingestion of the antiepileptic drug, Depakote¹, during her pregnancy with her daughter, M.B.D. Currently pending before the Court are five *Daubert* motion filed by Defendants and one *Daubert* Motion filed by the Plaintiffs contesting the admissibility of three experts.² Defendants move the Court to exclude the expert opinions of Dr. Michael Privitera (Doc. 155), Dr. Howard Saal (Doc. 157), Dr. Suzanne Parisian, (Doc. 156), Dr. C. Ralph Buncher (Doc. 153), and Dr. David Madigan (Doc. 154). Plaintiffs move the Court to exclude in part the proffered expert opinions of Dr. Anthony Scialli, Dr. Max Wiznitzer, and Dr. Stephanie Greene (Doc. 136).

For the reasons that follow, the Court will **GRANT IN PART AND DENY IN PART** Defendants’ Motion to Exclude the Expert Testimony of Dr. Michael Privitera (Doc. 155), Dr. Howard Saal (Doc. 157), Dr. Suzanne Parisian (Doc. 156), Dr. C. Ralph Buncher (Doc. 153), and Dr. David Madigan (Doc. 154). The Court will **GRANT IN PART AND DENY IN PART**

¹ “Depakote” refers to Abbott’s group of prescription drugs with the basic active ingredient valproic acid. Depakote is also sometimes referred to by the chemical names “valproic acid,” “valproate,” or “divalproex sodium.” Depakote is an anti-epilepsy drug (“AED”) that has been marketed by Abbott in the United States in some form since 1978.

² Although Plaintiffs’ Motion contains objections to four experts, on August 24, 2015, Plaintiffs filed a Notice of Withdrawal of Plaintiffs’ Motion to Exclude the Proffered Opinions of Dr. Kwame Anyane-Yeboah (Doc. 256). Accordingly, the Court will not consider Plaintiffs’ withdrawn objections regarding Dr. Kwame Anyane-Yeboah’s testimony.

Plaintiffs' Motion to Exclude in Part Proffered Expert Opinions of Dr. Anthony Scialli, Dr. Max Wiznitzer, and Dr. Stephanie Greene (Doc. 136).

Although the parties have requested oral argument on the *Daubert* motions, the Court may exercise its discretion in determining whether to rule on *Daubert* motions without a hearing where the issues have been fully briefed and there is an adequate basis in the record from which to determine reliability and validity of the proffered expert testimony. *See Nelson v. Tenn. Gas Pipeline Co.*, 243 F.3d 244, 249 (6th Cir. 2001) (holding that whether to hold a *Daubert* hearing is within a district court's discretion, where the issues are fully briefed" and there is an "adequate basis" in the record "from which to determine the reliability and validity" of the expert testimony) (relying upon *Greenwell v. Boatwright*, 184 F.3d 492, 498 (6th Cir. 1999)). In this case, the parties have developed an extensive record, including depositions. Because the *Daubert* issues have been well-briefed and the record is extensive, the Court will exercise its discretion to rule on *Daubert* motions without a hearing or oral argument.

I. LEGAL STANDARDS

A. Rule 702 of the Federal Rules of Evidence

Rule 702 of the Federal Rules of Evidence addresses the admissibility of expert witness testimony:

A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:

- (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
- (b) the testimony is based on sufficient facts or data;
- (c) the testimony is the product of reliable principles and methods; and
- (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. “A district court’s task in assessing evidence proffered under Rule 702 is to determine whether the evidence ‘both rests on a reliable foundation and is relevant to the task at hand.’” *Newell Rubbermaid, Inc. v. Raymond Corp.*, 676 F.3d 521, 527 (6th Cir. 2012) (quoting *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597 (1993)). The district court acts as a “gatekeeper” in making these determinations and must evaluate relevancy and reliability with “heightened care.” *United States v. Cunningham*, 679 F.3d 355, 380 (6th Cir. 2012) (citation omitted). The district court must perform its gatekeeper function before the testimony can be admitted regardless of whether the testimony is based on scientific knowledge, technical knowledge, or other specialized knowledge. *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 141, 147–49 (1999); *see also Mike’s Train House, Inc. v. Lionel, L.L.C.*, 472 F.3d 398, 407 (6th Cir. 2006).

The Sixth Circuit notes that “rejection of expert testimony is the exception, rather than the rule.” *In re Scrap Metal Antitrust Litig.*, 527 F.3d 517, 530 (6th Cir. 2008) (citation removed). As such, “Rule 702 should be broadly interpreted on the basis of whether the use of expert testimony will assist the trier of fact.” *Morales v. Am. Honda Motor Co., Inc.*, 151 F.3d 500, 516 (6th Cir. 1998) (citation removed). The trial court’s role as a gatekeeper of expert testimony is not meant to serve as a replacement of the adversary system. *See Burgett v. Troy-Bilt LLC*, 579 Fed. App’x 372, 377 (6th Cir. 2014) (citation removed).

As to reliability, the Supreme Court in *Daubert* identified several factors which might bear on a reliability determination: testing, peer review, publication, known or potential rate of error, and general acceptance. *Daubert*, 509 U.S. at 593–94. The *Daubert* factors are neither definitive nor exhaustive and may not apply in every case. *Mike’s Train House*, 472 F.3d at 407. “Red flags that caution against certifying an expert include reliance on anecdotal evidence,

improper extrapolation, failure to consider other possible causes, lack of testing, and subjectivity.” *Newell Rubbermaid*, 676 F.3d at 527. However, an evaluation of the reliability of an expert opinion does not involve a determination of whether the opinion is correct. *In re Scrap Metal*, 527 F.3d at 529–30; *GED Integrated Solutions, Inc. v. Durotech Int’l, Inc.*, No. 5:06CV1327, 2009 WL 233872, at *4 (N.D. Ohio Jan. 30, 2009) (citing *In re Scrap Metal*).

In certain cases, an expert’s experience alone may provide a reliable basis for his testimony. Fed. R. Evid. 702 (2000 Amendments advisory committee notes); *see also Campbell v. City of Springboro, Ohio*, 788 F. Supp. 2d 637, 662 (S.D. Ohio 2011) (stating that reliability concerns may focus on personal knowledge and experience). “If the witness is relying solely or primarily on experience, then the witness must explain how that experience leads to the conclusion reached, why that experience is a sufficient basis for the opinion, and how that experience is reliably applied to the facts.” Fed. R. Evid. 702 (2000 Amendments advisory committee notes); *see also Surles ex rel. Johnson v. Greyhound Lines, Inc.*, 474 F.3d 288, 296 (6th Cir. 2007) (quoting the advisory committee notes).

Rule 702 “does not require anything approaching absolute certainty.” *Tamraz v. Lincoln Elec. Co.*, 620 F.3d 665, 671 (6th Cir. 2010). However, an expert’s opinion must amount to more than mere speculation. *Id.* The Sixth Circuit has excluded an expert’s opinion when it was based upon a “string” of speculations:

And where one person sees speculation, we acknowledge, another may see knowledge, which is why the district court enjoys broad discretion over where to draw the line. Yet, so long as there is a line, some forms of testimony may cross it, and that happened here. [The expert’s] opinion contains not just one speculation but a string of them: A suggests by analogy the possibility of B, which might also apply to C, which, if we speculate about D, could eventually trigger E, so perhaps that happened here. At some point, the train becomes too long to pull and the couplings too weak to hold the cars together.

Id. at 672 (internal citation omitted).

Courts have struggled to draw the line between expert testimony that should be excluded because it is unreliable and testimony that should be admitted despite weakness in its factual bases. The Sixth Circuit has instructed as follows:

[A]n expert's opinion . . . should be supported by good grounds, based on what is known. The expert's conclusions regarding causation must have a basis in established fact and cannot be premised on mere suppositions. An expert's opinion, where based on assumed facts, must find some support for those assumptions in the record. However, *mere weaknesses in the factual basis of an expert witness' opinion . . . bear on the weight of the evidence rather than on its admissibility.*

McLean v. 988011 Ontario, Ltd., 224 F.3d 797, 800–01 (6th Cir. 2000) (internal quotations and citations omitted) (emphasis added); *see also In re Gen. Motors OnStar Litig.*, No. 2:-CV-DT, 2011 WL 679510, at *8 (E.D. Mich. Jan. 12, 2011) (stating that an expert's failure to consider all available material goes to the weight of the expert's testimony), *report and recommendations adopted by*, No. 2:07-MDL-01867, 2011 WL 674727 (E.D. Mich. Feb. 16, 2011). “An expert need not consider every possible factor to render a ‘reliable opinion;’ rather the expert need only consider enough factors to make his or her opinion sufficiently reliable in the eyes of the court.” *In re Gen. Motors OnStar Litig.*, 2011 WL 679510, at *8 (internal citation and quotation omitted). “Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence.” *Daubert*, 509 U.S. at 595.

B. Rule 403 of the Federal Rules of Evidence

Also, Rule 403 of the Federal Rules of Evidence permits relevant evidence to be excluded if it is prejudicial:

The court may exclude relevant evidence if its probative value is substantially outweighed by a danger of one or more of the following: unfair prejudice, confusing the issues, misleading the jury, undue delay, wasting time, or needlessly presenting cumulative evidence.

Fed. R. Evid. 403. “Like all evidence, the admissibility of expert testimony is also subject to a . . . balancing of probative value against likely prejudice under Rule 403.” *United States v. Geiger*, 303 F. App’x 327, 329 (6th Cir. 2008). The Supreme Court has recognized that expert testimony can “be both powerful and quite misleading because of the difficulty in evaluating it” so the district court in weighing probative value versus prejudicial effect should “exercise[] more control over experts than over lay witnesses.” *Daubert*, 509 U.S. at 595 (quotation and citation omitted).

II. DEFENDANTS’ *DAUBERT* MOTIONS

The Court will first consider Defendants’ *Daubert* Motions. Defendants move the Court to exclude the expert opinions Dr. Michael Privitera (Doc. 155), Dr. Howard Saal (Doc. 157), Dr. Suzanne Parisian (Doc. 156), Dr. C. Ralph Buncher (Doc. 153), and Dr. David Madigan (Doc. 154). The Court will consider the admissibility of each expert’s opinions in turn.

A. Dr. Privitera

In its summary judgment order, the Court considered whether Dr. Privitera, a board certified neurologist, is qualified to testify as an expert and whether Dr. Privitera is qualified to opine about the adequacy of the Depakote label.³ *Rheinfrank v. Abbott Laboratories, Inc.*, No. 1:13-cv-144, 2015 WL 4743056, at *15–16 (S.D. Ohio Aug. 10, 2015). The Court held that Dr. Privitera is qualified as a neurologist, but:

³ Although the Court at that stage of the proceedings was most concerned about the admissibility of Dr. Privitera’s opinion concerning the adequacy of the label, the Court’s ruling ultimately did address Defendants’ three central objections to Dr. Privitera’s opinions. To briefly summarize, Defendants argued: (1) Dr. Privitera’s testimony on regulatory issues are beyond the scope of his expertise as a neurologist; (2) Dr. Privitera’s opinion that in 2003, the Depakote label should have been changed to indicate a complete contraindication for use in women of childbearing years, and that Defendants should have provided specific warnings to patients directly, exceeds his expertise and is inconsistent with his own practices; and (3) Dr. Privitera’s opinion that as of 2003, Defendants should have warned that Depakote increased the risk of developmental delay is irrelevant and unreliable. Plaintiffs responded that Dr. Privitera was qualified to opine about the inadequacies of the Depakote label and materials submitted to the FDA. Further, Plaintiffs argued his opinions are consistent with his practice, and his developmental delay opinions are both reliable and relevant.

Dr. Privitera is not qualified to opine on the regulatory aspects of the case, including whether Abbott was required to send a patient package leaflet directly to patients or whether Abbott's submissions to the FDA should have included certain materials. Similarly, testimony about what Defendants should have included in the label or what materials should have been submitted to the FDA falls outside the scope of his expertise, as it falls under the regulatory component and is speculative. Thus, Dr. Privitera also may not testify about whether Depakote should have been contraindicated for all women of childbearing years. On the other hand, testimony in which Dr. Privitera opines on the medical facts and science regarding the risks and benefits of Depakote and compares that knowledge with what was provided in the text of the labeling is admissible.

Id. at *16. The Court also stated that in light of its preemption ruling, in which the Court concluded that Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted, Dr. Privitera's opinion regarding a developmental delay warning is not admissible.

Id. at *16, n.18. This evidence is irrelevant to the claims at issue in light of the Court's preemption ruling.

B. Dr. Howard Saal

Dr. Howard Saal, a geneticist and dysmorphologist, has been M.B.D.'s treating physician since her birth. (Saal Dep., Doc. 125 at PageID 14606, 14610.) Dr. Saal received his M.D. from Wayne State University and has been licensed to practice medicine in Ohio since 1993. (Doc. 125-1 at PageID 14688.) He is board certified by the American Board of Medical Genetics in Clinical Genetics and Clinical Cytogenetics and by the American Board of Pediatrics in Pediatrics. (*Id.*) Since 2006, Dr. Saal has been a tenured Professor of Pediatrics at the University of Cincinnati College of Medicine and Cincinnati Children's Hospital Medical Center, Department of Pediatrics. (*Id.* at 14689.) He is Director of the Craniofacial Center at Children's Hospital Medical Center in Cincinnati, a position he has held since 1998. (*Id.*) Dr. Saal has served as the Medical Director of the Medical Genetics Residency Program at Cincinnati Children's Hospital Medical Center since 1996 and as the Medical Director for the Cytogenetics Laboratory at the facility since 1995. (*Id.*) He has been Medical Director for the

Genetics Counseling Program at the University of Cincinnati College of Medicine since 1993.

(*Id.*) Dr. Saal is the author and/or co-author of numerous scientific peer-reviewed publications on genetics and birth defects. (*Id.* at 14691.) The Court finds that Dr. Saal is well-qualified within his specialty based on his experience and education.

Briefly stated, Dr. Saal opines that M.B.D.’s injuries are congenital but not genetic in origin and were caused by valproic acid. (Doc. 125-1 at PageID14693.) Dr. Saal also opines about the adequacy of both the 2003 and 2013 Depakote label. (*Id.* at 14702.) He asserts that the 2003 Depakote label does not state that valproate is more teratogenic than other antiepileptic drugs (“AEDs”), that safer alternatives are available, that use in pregnancy is contraindicated, that Depakote should be used as a drug of last resort for women of childbearing years, and that women of childbearing years should be taking adequate forms of contraception while taking valproate. (*Id.* at 14705.)

1. Qualified to Testify About Inadequacies of the 2003 Depakote Label

Defendants do not dispute that Dr. Saal’s qualifications. However, Defendants contend that Dr. Saal lacks the training, skill, knowledge, or experience to testify about whether the 2003 Depakote label was adequate, because he does not treat patients for epilepsy and has not prescribed Depakote or other AEDs to an epileptic patient. Further, Defendants argue Dr. Saal is unfamiliar with regulatory guidelines for labeling prescription drugs and has no experience drafting pharmaceutical labels and obtaining Food and Drug Administration (“FDA”) approval, so he is unqualified to render opinions about what is required from a regulatory perspective, or about what information prescribers required from the label in considering whether to prescribe Depakote.⁴

⁴ Defendants contend Dr. Saal’s opinions about the 2013 Depakote label are inadmissible because he is unqualified to offer them and they do not fit the facts of this case. In its Order Ruling on Motions *in Limine*, the Court held that

Plaintiffs contend that Dr. Saal is qualified as a treating geneticist and dysmorphologist who deals with the resulting birth defects from valproate to opine about the adequacy of the Depakote label. Plaintiffs argue that there is no requirement that one must be a prescriber or have regulatory experience to discuss the content of product labels. According to Plaintiffs, cross-examination is the proper outlet for questions about Dr. Saal's experience.

The Court finds that Dr. Saal is well-qualified based on his experience as a geneticist and dysmorphologist to testify as to the medical facts and science and compare that information and data with the language of the 2003 Depakote label. Doctors are "fully qualified to opine on the medical facts and science regarding the risks and benefits of [drugs] ... and to compare that knowledge with what was provided in the text of labeling and warnings on the [drugs] in question." *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Prod. Liab. Litig.*, No. MDL 1203, 2000 WL 876900, at *11 (E.D. Pa. June 20, 2000). Although courts have found that prescribing and/or treating physicians are qualified to opine as to the adequacy of a drug label, Defendants have not cited any case law holding that this is a prerequisite to qualification as a medical expert testifying as to the adequacy of the drug-at-issue's label. *Compare In re Gadolinium-Based Contrast Agents Prods. Liab. Litig.*, MDL No. 1909, No. 1:08-GD-50000, 2010 WL 1796334, at *1 (N.D. Ohio May 4, 2010) (finding Dr. Fine, a nephrologist, qualified to interpret and offer opinions about scientific studies and therefore qualified to opine as to whether the drug label or Dear Doctor letters contained adequate information, inaccuracies, or omissions that could deprive or mislead physicians like himself who treated renally impaired patients about the risks associated with the administration of the product at issue) with *In re Diet Drugs*, 2000 WL 876900, at *11 (finding two doctors qualified to testify as to the label's completeness by

subsequent Depakote labels post-dating M.B.D.'s conception and birth are not relevant. (*See Order on Motions in Limine*, Doc. 275 at PageID 30270.) Thus, it follows that Dr. Saal's opinions regarding the adequacy or inadequacy of such labels are irrelevant and will not be admissible.

comparing the medical facts and science regarding risks and benefits of the drugs in question with what was provided in the text of the labeling and warnings). Accordingly, the Court is not persuaded that the fact that Dr. Saal does not treat patients with epilepsy or prescribe AEDs renders him unqualified to compare the medical data with information in the 2003 Depakote label.

However, although he is accomplished in his field, Dr. Saal is not an expert in FDA regulations. For example, he has never consulted with the FDA about content of safety-related information in the drug label or published on the appropriate content of safety-related information in a drug label. (Saal Dep., Doc. 125 at PageID 14609–10.) As such, Dr. Saal lacks the requisite expertise to opine as to the regulatory aspects of the case, including what “should” have been in the 2003 label and whether the drug “should” have been contraindicated for women of childbearing years, as this assumes regulatory knowledge.

2. Reliable Methodology

The Court will next consider whether to exclude Dr. Saal’s causation opinions on the basis that he did not employ a reliable methodology, an aspect of his opinion challenged by Defendants. Defendants argue Dr. Saal merely assumes that M.B.D.’s Chiari I malformation, Peters Anomaly, and microcephaly were caused by M.B.D.’s *in utero* exposure to Depakote. In addition, Defendants contend that phenobarbital, as a known teratogen, must be considered in Dr. Saal’s differential diagnosis in order for the methodology employed to be reliable. Defendants contend that Dr. Saal’s lack of research or analysis on this topic reveals that no methodology was used, and that he assumed that phenobarbital played no role in M.B.D.’s injuries.

Plaintiffs contend that Dr. Saal has a reasonable basis for his opinion that M.B.D.'s birth defects are caused by Depakote, and the fact that Dr. Saal does not believe phenobarbital caused M.B.D.'s injuries does not make his methodology unreliable. Plaintiffs also argue Dr. Saal has reliable support for his opinions that Depakote caused M.B.D.'s Chiari I malformation and Peter's Anomaly.

Dr. Saal has relied upon differential diagnosis to assess causation in this case, which is an accepted method for determining causation. Differential diagnosis is:

[t]he method by which a physician determines what disease process caused a patient's symptoms. The physician considers all relevant potential causes of the symptoms and then eliminates alternative causes based on a physical examination, clinical tests, and a thorough case history.

Hardyman v. Norfolk & W. Ry. Co., 243 F.3d 255, 260 (6th Cir. 2001) (citing FEDERAL JUDICIAL CENTER, *Reference Manual on Scientific Evidence* 214 (1994)). The Fourth Circuit described the differential diagnosis methodology as follows:

Differential diagnosis, or differential etiology, is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated. *See Baker v. Dalkon Shield Claimants Trust*, 156 F.3d 248, 252–53 (1st. Cir. 1998). A reliable differential diagnosis typically, though not invariably, is performed after “physical examinations, the taking of medical histories, and the review of clinical tests, including laboratory tests,” and generally is accomplished by determining the possible causes for the patient's symptoms and then eliminating each of these potential causes until reaching one that cannot be ruled out or determining which of those that cannot be excluded is the most likely.

Id. at 260–61 (citing *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 262 (4th Cir. 1999)). The Sixth Circuit has held that a differential diagnosis is reliable and admissible where the doctor “(1) objectively ascertains, to the extent possible, the nature of the patient's injury, ... (2) ‘rules in’ one or more causes of the injury using a valid methodology, and (3) engages in standard diagnostic techniques by which doctors normally rule out alternative causes to reach a conclusion as to which cause is most likely.” *Monroe v. Novartis Pharm. Corp.*, 29 F. Supp. 3d

1115, 1122 (S.D. Ohio 2014) (citing *Best v. Lowe's Home Centers, Inc.*, 563 F.3d 171, 178 (6th Cir. 2009)).

Dr. Saal has satisfied the Sixth Circuit's standard with his differential diagnosis in his expert opinion. Dr. Saal's report describes embryonic developmental and how teratogens, such as valproate, can effect fetal development and cause a wide array of birth defects. (Doc. 125-1 at PageID 14693–97.) Dr. Saal notes that the epidemiology establishes that valproate disrupts fetal development and causes a wide array of serious fetal injuries. (*Id.* at 14699–701.) He also describes his care and treatment of M.B.D., in that he first evaluated M.B.D. when she was one day of age in neonatal ICU at Good Samaritan Hospital because of her cloudy corneas. (*Id.* at 14707–08.) At that time, Dr. Saal learned that M.B.D. was exposed to Depakote throughout Plaintiff Rheinfrank's entire pregnancy. (*Id.*) He suspected at that time that M.B.D.'s birth injuries were caused by valproate embryopathy. (Saal Dep. at PageID 14633, 14637.) Dr. Saal confirmed that diagnosis the next time he saw M.B.D. at three months of age. (*Id.* at 14633.)

Dr. Saal opines that M.B.D. has the features of Fetal Valproate Syndrome. (Doc. 125-1 at PageID 14708.) Dr. Saal opines that when a child is born with multiple birth defects, the child has a syndrome or identifiable pattern of defects that are pathogenetically related. (*Id.*) M.B.D. has undergone several tests to rule out genetic or inherited cause of birth defects, and based on the *in utero* exposure to Depakote and her multiple anomalies, including brain anomalies with Chiari I malformation, dysmorphic features, eye anomalies, small size, microcephaly, and low muscle tone, a diagnosis of Fetal Valproate Syndrome was made. (*Id.*) Dr. Saal also testified that M.B.D.'s injuries were not characteristic of phenobarbital exposure, and he excluded phenobarbital as the cause of her birth defects because phenobarbital does not cause the pattern of malformations that he saw in M.B.D. (Saal Dep., Doc. 125 at PageID 14628.)

The fact that Dr. Saal testified that M.B.D.’s birth defects are not characteristic of phenobarbital exposure does not render his causation opinion unreliable. As the Sixth Circuit has recognized, “doctors need not rule out every conceivable cause in order for their differential-diagnosis-based opinions to be admissible.” *Best*, 563 F.3d at 181; *Sheffer v. Novartis Pharm. Cop.*, No. 3:12-cv-238, 2013 WL 5276558, at *6 (S.D. Ohio Sept. 18, 2013) (failure to conclusively rule out every possibly alternative cause does not necessarily render expert testimony deficient under *Daubert*). Rather, the fact that other potential causes may remain “uneliminated” goes to the accuracy of the conclusion, not the soundness of the methodology, and would be properly addressed on cross-examination. *See Jahn*, 233 F.3d at 390.

Defendants raise other issues that are aimed at the weight of the evidence, as opposed to the admissibility of it. Briefly summarized, Defendants also argue that Dr. Saal cited, relied upon, and then ignored the only epidemiological study seeking to identify a causal connection between Depakote and microcephaly. Defendants also contend Dr. Saal has no reliable epidemiological support for his proposition that Depakote causes Chiari I malformation and Peters Anomaly. Finally, Defendants argue Dr. Saal’s opinion that Depakote is the most teratogenic of all commonly prescribed AEDs is not grounded in reliable methodology. Defendants claim that he is not qualified to offer these opinions, but in any event, he has cherry-picked favorable literature to rely upon and ignored contra authority. The objections raised by Defendants are appropriate for cross-examination, but are not a basis for exclusion. “Disputes as to the strength of [an expert’s] credentials, faults in [the expert’s] use of differential etiology as a methodology, or lack of textual authority for [the expert’s] opinion, go to the weight, not the admissibility, of [the expert’s] testimony.” *Monroe*, 29 F. Supp.3d at 1122 (citing *McCulloch v. H.B. Fuller Co.*, 61 F.3d 1038, 1044 (2d Cir. 1995)). “Vigorous cross-examination, presentation

of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence.” *Daubert*, 509 U.S. at 596.

C. Dr. Suzanne Parisian

Plaintiffs proffer the opinions of Dr. Suzanne Parisian, a medical doctor who is board certified in Anatomic and Clinical Pathology and has a master’s degree in biology. (Doc. 80-2 at PageID 1699.) Dr. Parisian is a former FDA Medical Officer, having served from 1991 to 1995 as a Commissioned Officer in the U.S. Public Health Service, where she achieved the rank of Lieutenant Commander and was primarily assigned to the Center for Devices and Radiological Health at the FDA. (*Id.*) She was also concurrently assigned clinical responsibilities at the Armed Forces Institute of Pathology, Office of the Medical Examiner for the Armed Forces. (*Id.*)

From 1991 to 1993, Dr. Parisian served as an FDA Medical Officer in the Office of Health Affairs, where she provided regulatory support to both the FDA’s Office of Compliance and Office of Device Evaluation. (*Id.*) There, Dr. Parisian’s responsibilities included health hazard and health risk assessment, safety alert and physician and layperson communications, review of adverse event reports (“AER”), and medical literature and review of product labeling, promotions, advertising and corporate records. (*Id.*) As to compliance with the Food Drug and Cosmetic Act (“FDCA”), Dr. Parisian was responsible for the review of mandatory adverse event reports submitted by manufacturers, as well as the review of reports voluntarily submitted directly to the FDA by health care providers, patients, and others. (*Id.*) Dr. Parisian presided over 162 health risk assessments convened to advise the FDA on overall health risk issues for the public. (*Id.*) Along with others, Dr. Parisian made recommendations to the FDA regarding

regulatory actions that should be undertaken by the FDA, health care providers, user groups, and manufacturers to help protect the public's welfare. (*Id.*)

From April through December 1993, Dr. Parisian was a Medical Officer in the Office of Device Evaluation at the FDA. (*Id.* at 1700.) As a Chief Medical Officer, she was involved in the review of proposed clinical trials, premarketing applications and training new medical officers and scientific reviewers. (*Id.*) Dr. Parisian was also an initial instructor at the FDA's Staff College, where she trained FDA reviewers in the design and evaluation of clinical data in investigational and premarketing applications. (*Id.*) Dr. Parisian has written a text book about the FDA, FDA Inside and Out. (*Id.* at 1699.) Currently, she consults regarding FDA regulatory matters, including premarket clearance, clinical trial design, and product labeling. (*Id.* at 1702–03.)

The Court, heeding the well-reasoned analysis of other courts determining whether Dr. Parisian is a qualified expert, finds that Dr. Parisian is well-qualified based on her experience, particularly her time spent as a Medical Officer for the FDA, to offer testimony about regulatory requirements relating to the development, testing, marketing, and surveillance of prescription drugs. *See Reece v. Astrazeneca Pharm., L.P.*, 500 F. Supp. 2d 736, 744 (S.D. Ohio 2007) (finding Dr. Parisian qualified to testify as to regulations governing the approval, labeling, advertising, and marketing of pharmaceutical and medical products, processes by which the FDA determines the efficacy and safety of new drugs and new drug applications, the issues the FDA considers in the development of product labeling and marketing information, and a manufacturer's responsibility within this system); *In re Gadolinium-Based Contrast Agents Prod. Liab. Lit.*, 2010 WL 1796334, at *13 (finding Dr. Parisian qualified to testify about regulatory requirements relating to development, testing, marketing, and surveillance of

prescription drugs); *In re Fosamax Prod. Liab. Litig.*, 645 F. Supp. 2d 164, 191 (S.D. N.Y. 2009) (same).

Defendants argue that Dr. Parisian should be precluded from testifying that Abbott did not adequately communicate safety risks to health care providers. According to Defendants, Dr. Parisian’s opinions are not based on any rule or regulation and amount to her personal interpretation of Abbott’s internal documents. Plaintiffs assert that Dr. Parisian’s report clearly references 21 C.F.R. § 314.81 as a basis for her opinions. The Court has found and agrees that Dr. Parisian may opine as to what actions Abbott could have taken and/or was required to take with respect to communicating risks to healthcare professionals.

1. Opinions Outside the Scope of Expertise

Dr. Parisian attempts to opine about matters outside the scope of her expertise, which the Court will not permit. Specifically, in her report, Dr. Parisian opines that certain birth defect risks were “knowable” to Abbott prior to 2003. She states that she bases this opinion on clinical experience, animal and scientific data, and other relevant evidence of mechanisms for possible risk. (Doc. 80-2 at PageID 1705.) In short, Dr. Parisian opines that had Abbott fulfilled its obligation to study Depakote, the information widely accepted concerning Depakote’s teratogenicity would have been known and warned of years sooner. (Parisian Dep., Doc. 80 at PageID 1557–58.) Although Dr. Parisian is qualified to opine about pharmacovigilance practices, including that Abbott could have created a pregnancy registry to study its drug and that results about the risks of the drug could have or might have been achievable sooner, she is not qualified to opine that certain risks of Depakote *would* have been known by 2003 had Abbott conducted research sooner or in a different manner. As Defendants point out, Dr. Parisian has no specialized expertise in the design of epidemiology studies or the design and interpretation of

pregnancy registries. (*Id.* at 1561.) Furthermore, the Court finds that testimony that Abbott would have known certain risks had it studied its drug differently or sooner to be speculative.

The Court also finds Dr. Parisian unqualified to opine that as of 2003, Depakote was known to be the most teratogenic drug. Dr. Parisian is not a teratologist and does not have any specialized knowledge or experience in evaluating AEDs. (*Id.* at 1549.) This opinion falls outside the scope of her expertise and is not admissible.

2. Motive, Intent, and/or State of Mind

Dr. Parisian will also not be permitted to testify as to the “knowledge, motivations, state of mind, or purposes” of Abbott, its employees, the FDA, or FDA officials. *See In re Fosamax Prod. Liab. Litig.*, 645 F. Supp. 2d at 192 (precluding Dr. Parisian from testifying as to knowledge, motivations, intent, state of mind, or purposes of the manufacturer, its employees, the FDA, or FDA officials). Dr. Parisian’s regulatory expertise does not give her the ability to read minds. This is not the proper subject for expert or lay testimony. *Id.*

3. Narrative History

Defendants also object to Dr. Parisian providing a narrative history of Depakote. This argument is well-taken. An expert “cannot be presented to the jury solely for the purpose of constructing a factual narrative based upon record evidence.” *Id.* (citing *Highland Capital Management, L.P. v. Schneider*, 379 F. Supp. 2d 461, 469 (S.D. N.Y. 2005) (precluding Dr. Parisian from testifying about narrative history)). As in *Fosamax*, “Dr. Parisian’s commentary on documents and exhibits will be limited to explaining the regulatory context in which they were created, defining any complex or specialized terminology, or drawing inferences that would not be apparent without the benefit of experience or specialized knowledge.” *Id.* “She will not

be permitted to merely read, selectively quote from, or ‘regurgitate’ the evidence.” *Id.* (citation omitted).

4. Warning of Developmental Delay

Furthermore, Dr. Parisian’s opinion that Abbott failed to warn of the risks of developmental delay is irrelevant in light of the Court’s summary judgment ruling and will not be admissible at trial.

5. Accutane and Thalidomide

Defendants also object to Dr. Parisian’s recitation of the regulatory histories of Accutane and Thalidomide and opinion that Abbott should have implemented the same or similar distribution restrictions as those implemented for Accutane and Thalidomide. The Court held in its Order Ruling on Motions *in Limine* that “evidence of how manufacturers of Thalidomide or Accutane acted to create public awareness of the teratogenic effects of their drug . . . is relevant to the issue of whether the warnings and instruction for Depakote were adequate.” (Order, Doc. 275 at PageID 30282.) However, the evidence “may not be used to show similarity” amongst those drugs and Depakote, as they are distinct and have different risk-benefit profiles. (*Id.*) Accordingly, Dr. Parisian may discuss how other drug manufacturers warned of the risks of teratogenicity as examples of what Abbott *could* have implemented, but she may not opine that Abbott *should* have implemented the same methods. Moreover, Dr. Parisian may not compare Depakote to Thalidomide or Accutane, as these drugs have distinct risk-benefit profiles.

D. Dr. C. Ralph Buncher

Dr. C. Ralph Buncher has been a Professor of Biostatistics and Epidemiology at the University of Cincinnati in the Department of Environmental Health of the College of Medicine since 1973, earning Emeritus status in 2010. (Doc. 107-1 at PageID 9312.) He earned degrees

in the disciplines of biostatistics and epidemiology at the Massachusetts Institute of Technology (B.S., 1960) and Harvard University (ScD, 1967 – Doctor of Science). (*Id.*) Dr. Buncher created and built the division of Epidemiology and Biostatistics at the University of Cincinnati. (*Id.*) He served as Director of Graduate Education for the Department of Environmental Health at the University of Cincinnati College of Medicine from 2000 to 2010. (*Id.*) Dr. Buncher became a fellow of the American College of Epidemiology in 1983 and a Fellow of the American Statistical Association in 1997. (*Id.* at 9383.) He has published over 100 articles within his specialty and has been involved with several clinical trials. (*Id.* at 9382–95.) The Court finds Dr. Buncher is well-qualified based on his experience and education.⁵

1. Qualified to Testify Regarding Adequacy of Warning

Defendants argue Dr. Buncher should not be permitted to opine as to the adequacy and/or content of the Depakote label or what warning language the Depakote label should have included. According to Defendants, these opinions should be excluded because Dr. Buncher is not a doctor, has never prescribed Depakote, and has never treated a patient with epilepsy. Furthermore, Defendants claim Dr. Buncher has no relevant experience with the FDA labeling regulations.

The Court finds that Dr. Buncher, as a well-qualified epidemiologist, is qualified to opine on the medical facts and science regarding Depakote and compare that data to a Depakote label. *See In re Yasmin and Yaz (Drospirenone) Mktg., Sales Practice and Prod. Liab. Litig.*, MDL No. 2100, 2011 WL 6302573, at *11 (S.D. Ill. Dec. 16, 2011) (finding epidemiologist qualified to review science and compare that knowledge with the data in the product label). However, Dr.

⁵ In their Motion, Defendants object to Dr. Buncher opining as to specific causation. Plaintiffs respond that Dr. Buncher is not offering specific causation testimony. As such, Defendants have withdrawn their objection. (Doc. 201 at PageID 25973.)

Buncher has no specialized knowledge or expertise in the regulatory field, as he has never worked for the FDA, nor is he an expert on FDA labeling regulations. (*See* Buncher Dep., Doc. 107 at PageID 9002, 9046–47.) Consistent with its ruling on other experts who lack such regulatory knowledge, the Court finds that Dr. Buncher lacks the requisite expertise to opine as to the regulatory aspects of the case, including what “should” have been in the 2003 Depakote label and whether Depakote “should” have been contraindicated for women of childbearing years, as this assumes regulatory knowledge.

2. Motive, Intent, and/or State of Mind

Defendants argue Dr. Buncher’s testimony includes his repeated attempt to characterize or describe Abbott’s intent, motives, and/or state of mind. For example, Dr. Buncher stated: “[Abbott’s] priority appears to have been to protect its market share instead of protecting unborn children.” (Doc. 107-1 at PageID 9354.) Dr. Buncher’s opinions on Abbott’s motives, state of mind, and intentions, whether expressed in the form of opinion or presented as a summary of documents, are not admissible at trial. *Fletcher v. VanDyne*, No. 2:07-cv-325, 2009 WL 3789925, at *3 (S.D. Ohio Feb. 24, 2009) (“the Court will not permit the expert to speculate as to defendants’ states of mind”). This type of testimony is not only unhelpful to the jury but also prejudicial. Neither Dr. Buncher nor any expert will be permitted to opine about Abbott’s intent, motives, and/or state of mind.

Defendants also object to Dr. Buncher’s narrative or editorialized description of documents. The Court agrees that this narration is unhelpful to the jury, as members of the jury are capable of evaluating the evidence themselves. As such, the underlying facts should be offered to the jury directly, as opposed to being presented in narrative summaries, such as many of those offered by Dr. Buncher. *See, e.g., Wilhoite v. Bi-Lo, LLC*, No. 3:06-cv-32, 2007 WL

5117410, at *2 (E.D. Tenn. June 29, 2007) (acknowledging that it is well-settled that testimony directed solely to lay matters which a jury is capable of understanding and deciding without the expert's help usurps the role of the trial judge in instructing the jury or the role of the jury in applying the law to the facts before it.)

3. White Papers

Defendant objects to Dr. Buncher's opinions that Abbott made material omissions and misrepresentations in its communications with FDA concerning developmental delay in White Papers submitted to the FDA in 2005, 2007, and 2009. In light of the Court's summary judgment Order ruling on the issue of preemption, the Court finds that what Abbott could have and/or failed to submit to the FDA in support of their request for a developmental delay warning to be irrelevant. This evidence will not be admissible at trial.

4. Responsibilities or Ethical Duties of Pharmaceutical Manufacturers

Defendants object to Dr. Buncher opining as to "industry standards" or "industry ethics." For example, in his report, Dr. Buncher opines that "[c]ompanies engaged in the manufacture and sale of ethical pharmaceutical products owe a duty to avoid harm to the public." (Doc. 107-1 at PageID 9313.) Defendants argue these standards are nothing more than Dr. Buncher's say-so, and the jury will be instructed by the Court as to Abbott's legal duties, which are relevant to the case. The Court agrees; Dr. Buncher will not be permitted to opine as to the industry standard or ethical duties owed by pharmaceutical companies. He is not a regulatory expert, and, in addition, the standards to which Dr. Buncher refers are undefined and appear to be based on nothing more than personal opinion.

5. Off-Label Promotion

Dr. Buncher offers opinions regarding off-label promotion of Depakote; Defendants object to the admissibility of those opinions, arguing they are irrelevant and will not assist the trier of fact. The Court has ruled that Abbott's promotion of Depakote for off-label use of treating tonic-clonic seizures is relevant to the issue of Abbott's knowledge and the feasibility of strengthening its label. (Order, Doc. 275 at PageID 30284–85.) However, the Court agrees with Defendants that Dr. Buncher lacks marketing and regulatory expertise and therefore would not be an appropriate expert to opine as to whether Abbott's promotion of Depakote constituted off-label promotion.

E. Dr. David Madigan

Dr. David Madigan is a Professor of Statistics at Columbia University, where he is also the Executive Vice-President of Arts and Sciences and Dean of the Faculty. (Doc. 135-20 at PageID 19008.) Dr. Madigan received his bachelor's degree in Mathematical Sciences from Trinity College Dublin in 1984 and was awarded the College's golden medal. (*Id.*) In 1990, he received a Ph.D. in Statistics, also from Trinity College. (*Id.*) Dr. Madigan has consulted for various pharmaceutical companies and is an FDA consultant. (*Id.*) Dr. Madigan is an elected Fellow of both the Institute of Mathematical Statistics and the American Statistical Association, as well as the American Association for the Advancement of Science, and he was the 36th most cited mathematician worldwide from 1995-2005. (*Id.*) Drug safety is a significant research interest for Dr. Madigan, with a focus on development and application of statistical methods for pharmacovigilance. (*Id.*) He has published more than 150 technical papers on Bayesian statistics, biostatistics, pharmacovigilance, statistical graphics, Monte Carlo methods, computer-

assisted learning, information retrieval, and text mining. (*Id.*) The Court finds that Dr. Madigan is well-qualified based on his experience and education.

Dr. Madigan conducted an analysis of adverse events for valproate and comparative AEDs using the FDA's adverse event database to determine whether a signal for developmental delay from *in utero* exposure to Depakote existed. Dr. Madigan found that an early signal existed from at least the year 2000 that linked Depakote to developmental delay as well as to autism.

1. Relevance

Defendants object to the admissibility of Dr. Madigan's report and/or his testifying, because they argue the Dr. Madigan's report and opinions are irrelevant due to the Court's summary judgment ruling, in which the Court held that Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted.

The Court disagrees that the entirety of Dr. Madigan's report and testimony should be excluded. Dr. Madigan's report addresses Abbott's awareness of an association of an *in utero* exposure to Depakote and developmental delay and whether Abbott could have identified a signal by undertaking a data-mining analysis. This inquiry is relevant to whether Abbott exercised reasonable care in studying its drug. Furthermore, Dr. Madigan's opinion that evidence existed since the 1980's that Depakote could cause developmental delay is relevant, as causation is contested. Evidence that Depakote has an increased statistical rate of developmental delay adverse event reports compared to similar products is relevant to show Depakote's ability to cause developmental delay.

However, in light of the Court's preemption ruling, Dr. Madigan will not be permitted to testify as to whether Abbott's attempt to change the Depakote label to include a developmental

delay warning were mishandled, that Abbott should have included a developmental delay warning in its 2003-2004, or how the FDA would have responded to a quantitative statistical evaluation showing a safety signal for developmental delay. These opinions are not relevant, and, in addition, the latter is speculative.

The Court will allow Dr. Madigan to testify, but will also use a limiting instruction to prevent the jury from considering his testimony for whether Abbott should have included a warning for developmental delay in 2003, as that claim is preempted.

2. Reliability

Defendants object to Dr. Madigan's methodology, in which Dr. Madigan conducted a quantitative statistical analysis using what are commonly referred to as "data-mining" algorithms of the FDA adverse event reporting system database ("FAERS" or "AERS"). To conduct his analyses, Dr. Madigan used the programming language perl (for data preparation and analysis), the statistical software package R (version 3.1.0), and the QScan pharmacovigilance platform provided by DrugLogic Inc. (Reston, VA). (Doc. 135-20 at PageID 19019.) To identify VPA reports, Dr. Madigan searched reports containing the following names: Depakote, depakene, depakine, epilem, epival, depacon, valproate, valproex, and valproic. (*Id.* at 19020.) To identify developmental delay reports, he searched for reports containing the MedDRA preferred term "developmental delay" and ran analyses using for different definitions used by Abbott at different times. (*Id.*) Dr. Madigan also ran analyses that required an outcome containing the word "congenital," or an indication containing the word "pregnancy," or the presence of the preferred term "maternal drugs affecting foetus." (*Id.*) Dr. Madigan used three widely-used AED comparator drugs in his analyses, carbamazepine, lamotrigine, and phenytoin. (*Id.*)

The Court finds that Dr. Madigan's methodology is sufficiently reliable. Dr. Madigan's method, data mining in pharmacovigilance, is generally accepted in the medical community and has been found to be a reliable methodology in other courts. *See In re Fosamax (Alendronate Sodium) Prod. Liab. Litig.*, Nos. 11-5304, 08-08, 2013 WL 1558690, at *8–9 (D.N.J. April 10, 2013) (finding Dr. Madigan's use of data mining a reliable methodology to conduct his data mining analysis).

Defendants assert that historically, there has been a significant lag between the time the FDA receives an adverse event report and the time it is entered into the AERS database. Defendants argue that Dr. Madigan's opinion that the results of his data mining analysis could have been replicated earlier assumes that the adverse event reports that constitute the foundation of his opinion were available to Abbott prior to 2004. The Court finds that this issue is not one of methodology but of credibility, which is appropriately addressed on cross-examination.

Further, Defendants contend use of data-mining algorithms was not standard practice in the pharmaceutical industry prior to Plaintiffs' exposure to Depakote in 2003 and 2004. Thus, according to Defendants, Dr. Madigan's opinion that Abbott should have undertaken a data-mining analysis like the one he conducted is based on his conclusion that the analyses were standard practice in the pharmaceutical industry prior to the time of M.B.D.'s exposure to Depakote. Again, this is an issue more appropriately addressed by means of cross-examination, but it is not a basis for exclusion of Dr. Madigan's opinions. To reiterate the directive from the Supreme Court in *Daubert*, "[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Daubert*, 509 U.S. at 596.

III. PLAINTIFFS' DAUBERT MOTION

A. Dr. Anthony Scialli

Dr. Anthony Scialli is an Obstetrician-Gynecologist and Reproductive Toxicologist. (Doc. 129-1 at PageID 15246.) Dr. Scialli is an Adjunct Professor of Obstetrics and Gynecology and of Pharmacology and Physiology at Georgetown University and a Clinical Professor Obstetrics and Gynecology at George Washington University. (*Id.*) Dr. Scialli received his medical degree from Albany Medical College, Albany, New York in 1975, following which he completed a residency in obstetrics and gynecology at George Washington University in 1979. (*Id.*) Dr. Scialli completed a fellowship in Reproductive Toxicology from 1982 to 1984. (*Id.*) He is board certified by the American Board of Obstetrics and Gynecology, and has an active license to practice medicine in the District of Columbia. (*Id.*)

Dr. Scialli is Director for the Reproductive Toxicology Center, A Non-Profit Foundation. (*Id.*) The Center operates a database called REPROTOX, which is a reference source for information on the reproductive and developmental effects of chemical and other agents on all aspects of reproduction. (*Id.*) Dr. Scialli is the founding editor of the peer-reviewed journal *Reproductive Toxicology*, and he continues to serve as a reviewer for articles submitted to *Reproductive Toxicology* as well as for articles submitted to other scientific journals, including *Birth Defects Research*, *Obstetrics and Gynecology*, the *New England Journal of Medicine*, and the *American Journal of Obstetrics and Gynecology*. (*Id.*)

From 1983 to 2004, Dr. Scialli was a full-time faculty member at Georgetown University School of Medicine, achieving the ranks of Professor of Obstetrics and Gynecology and Professor of Biochemistry and Molecular Biology. (*Id.*) He was also Director of the Residency Program in Obstetrics and Gynecology at Georgetown University Hospital. (*Id.*) During the years leading up to the conception of M.B.D., Dr. Scialli was a practicing physician, providing

care and counseling to women contemplating the use of AEDs during pregnancy. (*Id.* at 15246–47.) He also taught medical students, residents, and other physicians during that time period about principles of teratology and about the use of AEDs during pregnancy. (*Id.*)

Dr. Scialli served as an advisor or consultant on the subject of developmental toxicology and reproductive medicine for organizations such as the FDA, the World Health Organization, and the Environmental Protection Agency. He has worked in numerous capacities for the FDA since 1987. (*Id.*) In 1997, Dr. Scialli was appointed as a consultant to the FDA Pregnancy Labeling Task Force, an effort to revise and clarify pregnancy labeling that is still ongoing. (*Id.* at 15247.) While on the Pregnancy Labeling Task Force, Dr. Scialli participated in developing a guidance document on evaluating the risks of drug exposure in human pregnancies written for reviewers with the purpose of indicating how to consider a new data for inclusion or non-inclusion in labeling. (*Id.*) He was also a reviewer for the FDA Guidance document on pregnancy registries. (*Id.*) Dr. Scialli has also taught FDA courses regarding pregnancy labeling and reproductive toxicology, and has served on advisory committees within the FDA, including on the Committee for Reproductive Health Drugs. (*Id.*) The Court finds that Dr. Scialli is well-qualified based on his education and experience.

Despite these qualifications, Plaintiffs argue that Dr. Scialli is unqualified to opine that Abbott complied with FDA requirements at all times, because this is beyond his expertise and contrary to law. For example, Plaintiffs note Dr. Scialli has never been a regulatory full-time employee of the FDA. (Doc. 129 at PageID 15192). Dr. Scialli testified in his deposition that he does not know what obligations a company has in regards to adverse events, nor does he know the regulations governing such responsibilities, other than submission of AERs to the FDA. (*Id.* at 15187.) Further, Dr. Scialli could not define the components of a pharmacovigilance plan and

was unaware if any drugs had ever been removed from the market based solely on adverse events. (*Id.* at 15187–88.) Defendants argue that Dr. Scialli’s experience renders him well-qualified to opine about regulatory matters regarding drug labeling, as he has had over twenty-five years’ of experience working as a Special Government Employee at the FDA, including as a consultant on the FDA’s Pregnancy Labeling Task Force. Further, Defendants contend that Plaintiffs oversimplify Dr. Scialli’s responses to deposition questions. For example, Plaintiffs highlight that Dr. Scialli has never been a full-time regulatory employee of the FDA or of a drug company, but Defendants point out that Dr. Scialli has worked both as a consultant to drug companies and as an employee of the FDA for years. (*Id.* at 15192.)

The Court finds that Dr. Scialli is qualified to testify regarding FDA regulatory matters concerning drug labeling. Questions regarding his experience go to Dr. Scialli’s credibility and may be addressed on cross-examination.

1. Peters Plus Diagnosis

Plaintiffs raise two other objections to Dr. Scialli’s testifying as a witness. First, Plaintiffs object to Dr. Scialli being qualified to diagnose Peters Plus syndrome. The Court will initially point out that there is a dispute as to whether Dr. Scialli went so far as to diagnose Plaintiff with Peters Plus. Defendants argue Dr. Scialli’s report does not include a diagnosis but that Dr. Scialli is ruling out Peters Plus syndrome on the differential diagnosis. The Court disagrees based on the plain language of Dr. Scialli’s report, which states: “No one was ruled out Peters Plus as the cause of [M.B.D.’s] defects, and based on the records it *appears to be the best diagnosis.*” (Doc. 129-1 at PageID 15249) (emphasis added). He also states: “[M.B.D.’s] constellation of symptoms is more consistent with a diagnosis of Peters Plus syndrome than with

the diagnosis of fetal valproate syndrome/embryopathy reflected in [M.B.D.'s] medical records.”
(*Id.* at 15255.)

Plaintiffs argue that Dr. Scialli is not qualified to diagnose M.B.D. with Peters Plus syndrome. Plaintiffs note that Dr. Scialli is not a geneticist, dysmorphologist, or pediatrician. (Scialli Dep., Doc. 129 at PageID 15156.) Dr. Scialli does not treat children or diagnose them with fetal abnormalities (with the exception of the penis). (*Id.*) For example, Dr. Scialli has never seen a person with Peter’s Anomaly or a Chiari limb malformation. (*Id.*) He has never diagnosed a child with fetal valproate syndrome or Peters Plus. (*Id.* at 15170.) Moreover, Dr. Scialli has never seen the Plaintiff M.B.D.; he admits he has never examined M.B.D. and did not rely on any photos of M.B.D. in reaching his opinions. (*Id.* at 15181.) In reaching his opinion, Dr. Scialli relied upon literature he has read about symptoms of Peters Plus and fetal valproate syndrome, and upon his experience as an OB/GYN. (*Id.* at 15171.) His opinion is based on a comparison of the reported features associated with Peters Plus and fetal valproate syndromes with the features M.B.D. presents. (Doc. 129-1 at PageID 15253–55.)

Defendants respond that Dr. Scialli is a medical doctor who need not be a geneticist to reach his opinion and that he is well-qualified to render his opinion about Peters Plus. Defendants refer to Dr. Scialli’s decades of experience as a practicing physician at Georgetown University Hospital and George Washington University Hospital providing care and counseling to women of childbearing years considering AEDs during pregnancy. Further, Dr. Scialli has demonstrated expertise in reproductive and developmental toxicology, and has four decades of experience in teratology and genetics. As such, they argue, Dr. Scialli is qualified to testify about whether M.B.D. meets the established criteria for a diagnosis of Peters Plus.

The Court will allow Dr. Scialli to use his expertise to opine about whether he believes M.B.D.'s characteristics align with a Peters Plus diagnosis based on his medical experience and training. Plaintiffs may use cross-examination to challenge Dr. Scialli's experience and his conclusions.

2. Adequacy of Warning

Plaintiffs also object to Dr. Scialli's offering an opinion on the adequacy of the label without offering an opinion as to the teratogenicity of Depakote. Dr. Scialli opines that the warnings in the Depakote label were scientifically justified warnings about the use of Depakote during pregnancy. (Doc. 129-1 at PageID 15249–50.) However, during his deposition, Dr. Scialli testified that he is not offering a causation analysis about whether valproate causes facial dysmorphisms or birth defects. (Scialli Dep., Doc. 129 at PageID 15159–60, 15162.) Plaintiffs argue that because Dr. Scialli has no opinion as to what the risks of the drug are, his methodology assessing the adequacy of the label is unsound.

Defendants argue there is no requirement that an expert testifying as to warning adequacy must also testify as to causation, citing cases in which experts were permitted to testify as to the adequacy of a warning without an issue being raised regarding the expert's underlying opinion as to causation. *See, e.g., Matthews v. Novartis Pharm. Corp.*, No. 3:12-cv-314, 2013 WL 5780415, at *20 (S.D. Ohio Oct. 25, 2013); *Piskura v. Taser Int'l, Inc.*, No. 1:10-cv-248-HJW, 2013 WL 3967323, at *7–9 (S.D. Ohio Jul. 31, 2013). The Court has found Dr. Scialli qualified to testify as an expert, and, like the other experts who opine as to the adequacy of the label, he is qualified to review the medical data and compare that data to the text of the label. Plaintiffs have identified a number of distinguishable cases that do not address the issue of whether a defense expert may opine as to the adequacy of a label when he does not have an opinion as to causation.

For example, Plaintiffs cite the failure to warn case, *Miller v. Pfizer, Inc.*, 196 F. Supp. 2d 1062, 1089 (D. Kan. 2002), where plaintiffs alleged the drug Zoloft caused suicide. The Court did not permit Dr. Healy, a practicing physician who prescribed Zoloft and who had written extensively of the dangers of SSRI-induced suicide, to testify as to the adequacy of the drug label. *Id.* The Court determined Dr. Healy unqualified to testify that Zoloft causes akathisia, which in turn causes suicide in depressed patients. *Id.* “The Court is therefore somewhat at a loss to determine what expert testimony Dr. Healy might offer on the subject of warnings. If the jury will hear no evidence that Zoloft causes suicide, it cannot possibly conclude that Zoloft labels do not adequately warn against the danger that Zoloft causes suicide.” *Id.* By contrast, here, Defendants are not required to prove Depakote causes certain birth defects (rather, this is Plaintiffs’ burden). The Court does not find it necessary for Defendants’ expert to disprove Plaintiffs’ alleged claims, or that Depakote causes or does not cause certain outcomes, in order to testify about the label’s adequacy.

Thus, any issues about how Dr. Scialli reached his conclusion about the label’s adequacy go to the credibility or weight of his opinion, and will be more appropriately addressed on cross-examination.

B. Dr. Max Wiznitzer

Dr. Max Wiznitzer is a pediatric neurologist at University Hospitals Rainbow Babies and Children’s Hospital in Cleveland, Ohio. (Doc. 128-1 at PageID 15040.) Dr. Wiznitzer has been on the UH Rainbow Babies and Children’s Hospital staff since 1986. (*Id.*) He is also Professor of Pediatrics and Neurology at the Case Western Reserve University School of Medicine. (*Id.*) Dr. Wiznitzer is board certified in pediatrics and neurology, with special qualifications in child neurology and neurodevelopmental disabilities. (*Id.*) Dr. Wiznitzer earned his bachelor’s degree

in medical education from Northwestern University and medical degree from Northwestern University School of Medicine. (*Id.*) He completed a residency in pediatrics and fellowship in developmental disorders at Children's Hospital Medical Center in Cincinnati, Ohio and a fellowship in pediatric neurology at Children's Hospital of Philadelphia. (*Id.*) He also completed postdoctoral training as a National Institutes of Health National Research fellow in higher cortical functions at Albert Einstein College of Medicine in the Bronx, New York. (*Id.*) Dr. Wiznitzer has authored or co-authored 11 textbook chapters and nearly 70 scientific papers in medical journals. (*Id.*) The Court finds Dr. Wiznitzer to be well-qualified based on his experience and education.

Plaintiffs move the Court to preclude Dr. Wiznitzer from testifying about the adequacy of the Depakote label.⁶ Plaintiffs contend that like Dr. Scialli, Dr. Wiznitzer offers an opinion as to the adequacy of the Depakote warning without having formed an opinion as to whether Depakote causes birth defects. (Wiznitzer Dep., Doc. 128 at PageID 15011.) As with Dr. Scialli, the Court does not find that this is a valid basis to exclude Dr. Wiznitzer's testimony regarding the adequacy of the label. Dr. Wiznitzer is qualified based on his education and experience to review the medical data and compare that data with the language in the label. Dr. Wiznitzer testified that he reviewed numerous articles in the past regarding the teratogenic effects of Depakote and has known for years the risks of defects. (*Id.* at 15011, 15020.) Dr. Wiznitzer also testified that his opinions are based on his training and education, which includes prescribing Depakote and other AEDs. (*Id.* at 15011, 15014.) Further, although Plaintiffs also object to the number of articles Dr. Wiznitzer reviewed, the Court finds this is an issue of credibility and weight of testimony, as opposed to admissibility.

⁶ Plaintiffs originally also objected to Dr. Wiznitzer offering an opinion about autism on the basis that it would be irrelevant. Defendants agreed that it will not offer any opinions on autism by Dr. Wiznitzer, as Plaintiff have stated that they are not pursuing a claim for autism or autism spectrum disorder. (Doc. 186 at PageID 24690.)

Plaintiffs also object to Dr. Wiznitzer opining that “[b]eginning in 1996, these Depakote warnings were included in a black box. These warnings clearly advised prescribing physicians that severe teratogenic effects could occur in the offspring of mothers who took Depakote during pregnancy.” (Doc. 128-1 at PageID 15044.) In responding to a question in his deposition regarding this statement and whether he was holding himself out as representing what prescribing physicians everywhere knew about the risks of Depakote as of 1996, Dr. Wiznitzer stated he was holding himself out as to what neurologists knew or should have known as of 1996. (Doc. 128 at PageID 15017.) The Court agrees with Plaintiffs that Dr. Wiznitzer is not qualified to opine about the medical community’s state of mind. *See Pfizer Inc. v. Teva Pharm. USA, Inc.*, 461 F. Supp. 2d 271, 278 (D.N.J. 2006) (doctor not permitted to testify concerning what all doctors generally consider when making prescription decisions, what all physicians believe or knew about the risks and benefits of drug category at issue, or the extent to which marketing drove the drug’s prescriptions.) Accordingly, Dr. Witnizter’s conclusion about what was known or knowable to the medical community in 1996 is beyond the scope of his expertise and will not be admissible.

C. Dr. Stephanie Greene

Dr. Stephanie Greene is a pediatric neurosurgeon on the faculty of the University of Pittsburgh Medical School in the Department of Neurological Surgery. (Doc. 127-1 at PageID 14959.) Since 2009, Dr. Greene has been on staff in the Pediatric Neurosurgery Division at Children’s Hospital at Pittsburgh. (*Id.*) Dr. Greene graduated from Dartmouth College in 1993, with a degree in biology and psychology and a concentration in neuroscience. (*Id.*) She obtained her medical degree from Albany Medical College and completed her neurosurgical residency at Harvard University in the Brigham & Women’s and Children’s Hospital Boston

Program. (*Id.*) She completed a fellowship in pediatric neurosurgery through the University of Washington Program at Seattle Children’s Hospital in 2005. (*Id.*) Dr. Greene is certified by the American Board of Neurological Surgery (May 2009) and by the American Board of Pediatric Neurological Surgery (November 2010). (*Id.*) She has authored over forty journal articles, abstracts and book chapters. (*Id.*) The Court finds Dr. Greene is well-qualified based on her experience and education.

Plaintiffs argue that as a neurosurgeon, Dr. Greene lacks the education, training or experience to determine the cause of Plaintiff M.B.D.’s Chiari I malformation. Dr. Greene is not a geneticist, teratologist, or dysmorphologist, or reproductive toxicologist. (Doc. 127 at PageID 14940.) She is involved in the diagnosis of craniosynotosis, but it is the only facial dysmorphism with which she is involved. (*Id.*) She is not involved in attributing any facial dysmorphisms or other fetal anomalies to a particular syndrome. (*Id.*)

Defendants respond that Dr. Greene is well-qualified to offer an opinion as to the cause of M.B.D.’s Chiari I malformation. She has treated over 6,000 patients with Chiari I malformation and routinely develops a birth history, screening her patients and their mothers, to determine their history with respect to exposures to drugs, alcohol, tobacco, and teratogens *in utero*. (Greene Dep., Doc. 127-1 at PageID 14952, 14944–45.)

The Court agrees with Defendants that Dr. Greene need not have diagnosed a patient with Chiari I malformation to opine as to the cause of it in this case. The Court is satisfied that Dr. Greene’s experience and education, and in particular, her having treated over 6,000 patients with Chiari I malformation, is enough to qualify her to opine as to the cause of Plaintiff’s Chiari I malformation in this case. As with all experts, cross examination is an appropriate means to challenge Dr. Greene’s experience or conclusions.

Plaintiffs also challenge Dr. Greene's methodology, arguing that Dr. Greene's testimony is unreliable because she failed to rely upon a valid, scientific methodology. Dr. Greene testified that her opinions were formed with a combination of literature review and her own clinical practice. (Doc. 127 at PageID 14952.) Plaintiffs argue her review of literature was not exhaustive and she does not have sufficient clinical experience. Plaintiffs argue that though Dr. Greene has had thousands of patients with Chiari I malformation, she did not review the records of a single case before testifying, and she failed to conduct an internal review of her own patients' files to identify cases of Chiari I malformation associated with Depakote exposure. (*Id.* at 14939.) The issues raised by Plaintiffs are again more appropriately addressed on cross-examination, as they touch about the credibility of Dr. Greene's testimony, as opposed to its admissibility.

IV. CONCLUSION

For the foregoing reasons, the Court **GRANTS IN PART AND DENIES IN PART** Defendants' Motion to Exclude the Expert Testimony of Dr. Michael Privitera (Doc. 155), Dr. Howard Saal (Doc. 157), Dr. Suzanne Parisian (Doc. 156), Dr. C. Ralph Buncher (Doc. 153), and Dr. David Madigan (Doc. 154). The Court **GRANTS IN PART AND DENIES IN PART** Plaintiffs' Motion to Exclude in Part Proffered Expert Opinions of Dr. Anthony Scialli, Dr. Max Wiznitzer, and Dr. Stephanie Greene (Doc. 136).

IT IS SO ORDERED.

____s/Susan J. Dlott_____
Judge Susan J. Dlott
United States District Court